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EXAMINER	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/965,610
Filing Date: September 26, 2001
Appellant(s): CANTOR ET AL.

Robert W. Sprague
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed November 10, 2008 appealing from the Office action mailed March 26, 2008.

The receipt is acknowledged of applicants' IDS filed 01/22/2009. An initialized and signed copy of 1449 form is attached to this examiner answer.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

WO 96/08229	Minnesota Mining and Manufacturing Company	3-1996
US 5,993,849	Assmus et al.	11-1999

(9) Grounds of Rejection

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1-9, 16-18, 28-31, 35-37, 39-47 and 52-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/08229 ('229) by itself or in view of US 5,993,849 ('849).

WO '229 teaches a transdermal drug delivery device comprising a backing and a matrix comprising a copolymer, a softener and a drug (page 2, lines 5-23). The copolymer comprises 40-90% of one or more A monomers selected from the group consisting of alkyl acrylates containing 4 to 10 carbon atoms in the alkyl group and alkyl methacrylates containing 4 to 10 carbon atoms in the alkyl group and up to 60% of one or more ethylenically unsaturated B monomers copolymerizable with the A monomers. The composition further comprises more than 30% of a macromonomer copolymerizable with the A and B monomers (page 2, lines 5-23). The A monomers are taught on page 4, lines 3-14 with isooctyl acrylate preferred. The B monomers are taught on page 4, line 15 through page 5, line 12, with hydroxyethyl acrylate preferred. The macromonomers are taught on page 5, line 13 through page 8, line 28. Polymethylmethacrylate macromonomers are preferred (page 6, lines 17-18). The softeners of the delivery device affect skin penetration rate and include fatty acids, fatty alcohols, fatty acid esters such as methyl laurate and tetraglycols (page 8, line 29 - page 10, line 15). Softeners can be included in amounts up to 60% by weight of the matrix (page 10, lines 7-15). WO '229 further contemplates various drugs for delivery by the device including analgesics such as fentanyl (page 12, line 28). The drug is present in the transdermal device in an amount of about 0.01 to about 30 percent by weight (page 13, lines 16-18). Also, the drug is substantially fully dissolved, and the matrix is substantially free of solid undissolved drug (page 13, line 18-20). The transdermal device comprising the pressure sensitive adhesive disclosed by WO '229 allows

dissolution of drug and relatively heavy loading with oily excipients, maintains contact with skin, and can be removed cleanly from the skin (page 3, lines 11-15).

Although WO '229 listed fentanyl as a possible acceptable drug for transdermal delivery by the disclosed transdermal copolymer composition, however, WO '229 does not specifically exemplify fentanyl. The reference exemplifies nicotine and levonorgestrel. WO '229 recognized the suitability of fentanyl to be delivered transdermally in an adhesive copolymer of alkyl acrylate monomer and ethylenically unsaturated monomer.

US '849 teaches adhesive composition suitable for transdermal delivery systems and having improved tolerance on the skin and improved controlled release of the active substance (abstract; col.2, lines 15-19). The composition comprises acrylate copolymer and preferred drugs are exemplified by fentanyl and nicotine (claim 10). Therefore the art recognized the equivalency between nicotine and fentanyl in terms of drugs suitable for transdermal delivery from an acrylate copolymer composition.

Therefore, it would have been obvious to one having ordinary skill in the art at the of the invention to provide transdermal delivery composition comprising copolymer of alkyl acrylate monomer and ethylenically unsaturated monomer as disclosed by WO '229, and use the composition to deliver fentanyl, motivated by the teaching of WO '229 that transdermal device comprising the disclosed pressure sensitive adhesive copolymers allows dissolution of drug and relatively heavy loading with oily excipients, maintains contact with skin, and can be removed cleanly from the skin, with reasonable expectation of having transdermal delivery composition comprising copolymer of alkyl

acrylate monomer and ethylenically unsaturated monomer and fentanyl wherein the device allows dissolution of fentanyl, as desired by applicants, maintains contact with skin, and can be removed cleanly from the skin.

Additionally one having ordinary skill in the art at the time of the invention would have been motivated to provide transdermal delivery composition comprising copolymer of alkyl acrylate monomer and ethylenically unsaturated monomer as disclosed by WO ‘229, and use the composition to deliver fentanyl as disclosed by US ‘849, motivated by the teaching of US ‘849 that fentanyl is one of the preferred drugs to be delivered in acrylic copolymer adhesive as evident by reciting fentanyl in the claims, motivated by the teaching of US ‘849 that such a transdermal delivery system has improved controlled release of the active substance with reasonable expectation of having transdermal delivery composition comprising copolymer of alkyl acrylate monomer and ethylenically unsaturated monomer and fentanyl with improved controlled release rate of fentanyl.

(10) Response to Argument

Appellants argue that WO '229 disclosure is very general with respect to a transdermal formulation containing fentanyl and amount of drug that can be present, with lack of any emphasis on fentanyl, while the pending claims are directed to transdermal formulations containing a relatively high concentration of fentanyl. As the Examiner recognizes, WO '229 publication specifically illustrates delivery of nicotine. It is noteworthy that the Examiner concedes that the '229 publication fails to "specifically

exemplify fentanyl". The only mention of fentanyl is on page 10 in a paragraph that appears to be an attempt to list almost any and every type of drug. Appellants argue that '229 publication does not lead one skilled in the art to a finding that 8-30% fentanyl by weight would fully dissolve in the claimed formulations.

In response to this argument, it is argued that WO '229 teaches the claimed copolymer comprising drugs including fentanyl in a concentration encompassing the claimed concentration. WO '229 teaches that transdermal device comprising the disclosed pressure sensitive adhesive copolymers allows dissolution of drug. Therefore, the degree of solubility of fentanyl to the extent of 8-30% in the copolymer disclosed by the prior art is expected to be the same as instantly claimed copolymer, since compounds and their properties are not separable. WO '229 disclosed the same copolymer instantly claimed and recognized the suitability of the copolymer to deliver fentanyl and further teaches the capability of the copolymer to dissolve from 0.01 to 30% of the therapeutic agent. The disclosed examples and preferred embodiment do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). "A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. The degree of teaching away will of course depend on the particular facts; in general, a reference will teach away if it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant." *In re Gurley,*

27 F.3d 551,553 (Fed. Cir. 1994). In the instant case the WO '229 does not discourage one having ordinary skill in the art from delivering fentanyl in the disclosed copolymer, contrarily, it is suggested by the WO '229 that many drugs including fentanyl can successfully delivered by the copolymer of WO '229. In considering the disclosure of the reference, it is proper to take into account not only the specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom. *In re Preda*, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968). The rational to modify or to combine the prior art does not have to be expressly stated in the prior art; the rational may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art. The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve different problem. It is not necessary that the prior art suggest the combination or modification to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972).

Appellants argue that the alleged equivalency of nicotine and fentanyl which the Examiner points to in the '849 publication does not remedy this deficiency in the '229 publication. Nicotine and fentanyl are dissimilar and nicotine is not even a solid at room temperature. Moreover, the only mention of fentanyl in the ' 849 publication is in claim 10 which lists fentanyl and nicotine as members of a Markush group including other drugs. Happenstance mention of both fentanyl and nicotine in a diverse list of drugs

simply does not support the equivalency of fentanyl and nicotine. It is not understood how Naik et al. which compares bioavailability and pharmacokinetics of nicotine and fentanyl teaches anything about a formulation containing an acrylate copolymer and a high loading of dissolved fentanyl.

In response to this argument, it is argued that US '849 is relied upon to show that nicotine and fentanyl are equivalent in the term of both being able to be delivered transdermally, and both being able to be delivered from acrylate copolymer adhesive matrix, as also disclosed by WO '229. The article by Naik et al. demonstrates and compares properties, bioavailability and pharmacokinetics of nicotine and fentanyl but does not show or compare their behavior with acrylate copolymers in order to consider fentanyl and nicotine are distinct and cannot be delivered transdermally using the same polymers. A conclusion of obviousness under 35 U.S.C. 103 (a) does not require absolute predictability, only a reasonable expectation of success; and references are evaluated by what they suggest to one versed in the art, rather than by their specific disclosure. *In re Bozek*, 163 USPQ 545 (CCPA 1969). The disclosed examples and preferred embodiment do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971).

Additionally, it has been held that "When a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious." *KSR Int 'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740 (2007) (quoting *Sakraida v. AG Pro, Inc.,* 425 U.S. 273,282 (1976)). "When the question is whether a patent claiming the

combination of elements of prior art is obvious," the relevant question is "whether the improvement is more than the predictable use of prior art elements according to their established functions."

Appellants argue that Roy et al. is very pertinent to the allowability of the instant claims because this publication speaks directly to fentanyl/acrylate copolymer formulations and teaches that formulations containing over 4% fentanyl had undissolved fentanyl particles in addition to dissolved fentanyl. Thus Roy et al. is a clear teaching away from the formulations of the instant invention. Additionally, the sole acrylate adhesive disclosed in Roy et al., Gelva 737, is a copolymer containing 72% 2-ethylhexyl acrylate and 28% vinyl acetate that is recited in claim 1 of the instant application. The language at the end of that claim "wherein the composition is free of undissolved fentanyl" serves to exclude any formulation where the combination of copolymer and the amount of fentanyl are such that there is undissolved fentanyl in the formulation.

In response to these arguments, Roy et al. publication is directed to comparison of four different adhesives with regard to the permeation of fentanyl through the adhesives (acrylate, two types of silicones, and PIB) and with regard to the permeation of fentanyl from the different adhesives through the skin. Roy disclosed that acrylate has higher solubility to fentanyl than silicone and PIB, see the abstract. Roy et al. did not disclose any where that acrylate formulation containing over 4% fentanyl had undissolved fentanyl particles in addition to dissolved fentanyl. The article disclosed that PIB formulation having more than 4% fentanyl showed dispersed particles because PIB

reaches saturation of fentanyl at 4%. Since acrylate has fentanyl solubility more than PIB, then more than 4% can be dissolved in acrylate. Roy et al. disclosed that permeation of fentanyl was higher through acrylate and silicone than through PIB, page 493, and figure 2, and further teaches that the release rate of fentanyl from acrylate was 2-3 times higher than other adhesives. However, Roy still disclosed that even though the acrylate adhesive exhibited a relatively higher release rate in water, the skin fluxes from monolithic acrylate matrix was considerably lower than other adhesives, figure 4 and page 495. The relative low skin flux rate disclosed by Roy et al. would have been a motivation to one having ordinary skill in the art to add more than 4% fentanyl since Roy disclosed that acrylate has high fentanyl solubility in order to obtain higher skin flux rate. Further, Roy et al. in their study, they used determined amount of fentanyl in the four adhesives of the study for the purpose of comparison, bottom of right column of page 491, and they would not add more than 4% fentanyl because this is the limit for loading fentanyl in PIB and if more than 4% used, then PIB can not be part of the comparative study. In other words, Roy et al. used determined quantity of fentanyl and they did not attempt to compare more than 4% loading of fentanyl in the adhesive. Roy et al. did not try more than 4% with acrylate adhesive and would not even try to do so since PIB will not be part of the comparative study as it can not dissolve more than 4%. Additionally, it is noted that Roy et al. used Gelva 737 that is provided as solution of copolymer in ethyl acetate and toluene, and WO ‘229 uses the copolymer used by Roy et al. with the same solvent, see for example page 21, lines 4-6. Therefore the dissolution of fentanyl in the acrylate copolymer of WO ‘229 is expected to be the same as Roy et al. and no reason

provided by Roy et al. or WO '229 that the acrylate copolymer will not dissolve more than 4% of fentanyl.

Appellants argue that all pending claims directly or indirectly require presence of fentanyl in an amount of about 8-30% by weight and further require the composition be free of undissolved fentanyl.

In response to this argument, the examiner above response to the arguments against the cited references is hereby repeated. The dependent claims are obvious over the combination of WO '229 and US '849. A conclusion of obviousness under 35 U.S.C. 103 (a) does not require absolute predictability, only a reasonable expectation of success; and references are evaluated by what they suggest to one versed in the art, rather than by their specific disclosure. *In re Bozek*, 163 USPQ 545 (CCPA 1969).

In the light of the foregoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the claims would have been *prima facie* obvious within the meaning of 35 U.S.C. 103 (a).

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Isis A Ghali/

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